DEPARTMENT OF HEALTH AND HUMAN SERVICES

95160d

Food and Drug Administration
Cincinnati District Office
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VIA FEDERAL EXPRESS

January 10, 2005

Steven J. Berke, President/CEO
Cincinnati Sub-Zero Products
12011 Mosteller Road
Cincinnati, OH 45241-1528

WARNING LETTER CIN-05-24253

Dear Mr. Berke:

An inspection of your medical device manufacturing firm located in Cincinnati, OH was conducted by our investigators on November 8, 9, and 15, 2004. This inspection revealed that the devices manufactured at that facility, class II hypo/hyperthermic machines, are adulterated within the meaning of Section 501(h) of the Federal Food, Drug, and Cosmetic Act (the Act), in that the methods used in, or the facilities or controls used for, manufacturing, packing, storage, or installation are not in conformance with the Quality System Regulation (QSR), as specified in Title 21, Code of Federal Regulations (CFR), Part 820. In addition, the Warm Air 135 is misbranded within the meaning of Section 502(t) because you failed to provide reporting information required under Section 519 of the Act and 21 CFR Part 806. We acknowledge your letter dated November 24, 2004 responding to the FDA-483 Observations. Our review of the letter finds that it is inadequate to address the deficiencies noted during the inspection.

The deviations include, but are not limited to, the following:

Reports of Corrections and Removals (21 CFR 806)

1. You made a correction on the Warm Air 135 warming units, and took a corrective action but you did not notify the FDA or document a reason for not notifying FDA 21 CFR 806.20(b)(4).

Quality System Regulation (21 CFR 820)

2. A validated process was not reviewed and evaluated and revalidated when changes or process deviations occurred 21 CFR 820.75(c).

Specifically,
a) During the 8/29/03 validation of the Microtemp II, you made changes to the production procedure for manufacturing during validation. For example, you changed the order of the steps of production, added "use [redacted] to ruff up the membrane recess and clean it with [redacted] changed hose assembly size,

changed the need for attaching the ground wire, and added information on how to perform the wire hook up. This is not a complete list of changes. You failed to revalidate or document the reason for not revalidating.

b) On or about 6/22/04, you ran validation on the replacement of an O-ring on the Microtemp II. The Test Data Report documented test setup, test procedures and test results. You did not fill out objective, acceptance criteria, conclusion, disposition, and who analyzed the test until 11/9/04, approximatelv 3 1/2 months from the approved engineering change notice on 7/27/04.

c) On or about 8/10/04, validation of a new pump for the Microtemp II was run. Eleven of the 11 device history records used during the validation documented a water flow rate below the set specification of [redacted]. No additional testing was performed. You now use the new pumps, but there is no explanation of why the pump was accepted even though the devices failed to meet your specifications or you did not document your reason for changing the specification from [redacted]

In your November 24th response to FDA-483 Item #2, you do not address that eleven out of 11 history records for devices used in validation show that they were below the water flow rate specification but the devices were nonetheless deemed acceptable. It also appears that your devices could not meet the specification – so you just changed the specification without a justification or change notice. The December 2004 letter attempts to clarify this issue further. It does not describe the rationale for why the new specification more closely approximates actual conditions of use. Therefore, we are unable to assess the adequacy of your corrective action at this time.

3. **Finished devices that did not meet your specifications were distributed 21 CFR 820.80(d). Procedures for acceptance activities were not implemented 21 CFR 820.80(a). The justification for use of reworked product was not documented 21 CFR 820.90(b)(1).**

Specifically,

a) Nine of 21 Device History Records (DHR) required rework and had no approval for release. The Instruction procedure that applies to all the voltage types of the Microtemp II states that when rework is done QA should review for acceptance. The bottom of the device history record production/inspection sheet requires a QA signature and date for release on rework. (DHR- 034-7470032, 034-74700034, 034-74700037, 034-74700039, 041-74700310, 042-74700682, 043-74701105, 042-74700787, and 042-74700958.)

b) Five of 21 DHRs reviewed had different specifications for water flow testing. According to the Instruction procedure for the Microtemp II, the water system flow rates must be [redacted] gpm or greater. The procedure documents no change in the specification since the beginning of production on 9/11/03. DHR 034-7400032, 034-74700034, 034-74700037, and 034-74700039 have a specification of [redacted] gpm or greater. DHR 044-74701446 has a specification of [redacted] gpm or greater.

c) Four of 21 DHRs reviewed failed to have a complete documented inspection and were released. DHR 041-74700817 has no time run documented. DHR 041-74700310 has no leak test or electrical inspection documented on the original or rework test. DHR 042-74700787 has no cleaning inspection, final inspection, or quality release to ship. DHR 042-74700958 is marked as a retest, but the firm has no original production/testing report.

d) Four of 21 DHRs reviewed had two different production/inspection reports marked as originals. The first original DHRs were not kept in the DHR files and were copies, not originals. Each device required

rework and a retest sheet which documented the device passed all the tests. The originals found in the DHRs were dated the same as above, had the same serial numbers, but had different CPU/Power Supply Boards and did not show rework was needed. (DHR 034-74700032, 034-7470034, 034-74700037, and 034-7470039).

In your November 24th written response to FDA-483 Item #3, you state that each of the history records listed in this item have been reviewed and found acceptable. The FDA-483 item addresses units that failed your specifications or failed to have the results of tests documented. You have not explained in your letter how/why records showing devices that fall below specification or devices that have not been tested can be deemed acceptable. The December 2004 letter provides additional details. With respect to item 3d in your letter, your explanation of the problem does not appear to correspond to the records collected by the investigator. We cannot assess the adequacy of the corrective action for this item at this time.

4. **The procedures addressing documentation of corrective and preventive action activities were not implemented 21 CFR 820.100(b). You did not document the evaluation of whether an investigation of nonconforming product was necessary 21 CFR 820.90(a).**

Specifically,
a) You initiated a correction on the Warm Air 135 based on complaints 00296, 00651, 00752, but did not follow your procedure for initiating a corrective action.

b) Three of 17 Nonconformance Reports did not have an investigation or corrective action when needed.

1) Nonconformance Report (NCR) 0002722 documented blankets manufactured on a brand new machine and all of them failed testing. You stated that the design engineers had not developed and issued the new specification production sheets when manufacturing started. You did not investigate to determine why the machine was used without production specifications. Further, you did not document the investigation or justify why a Corrective Action was not initiated to prevent the nonconformance from recurring.

2) NCR 0003264 was documented because 15 Microtemp IIs were manufactured with a pump no longer in use and the 15 devices were reworked. There was no investigation to determine why the old pumps were in stock, not removed after design change, and used, but not found until devices were completely manufactured. Additionally, you did not justify why a Corrective Action was not issued.

3) NCR 0002829 had two different versions in the file. One report has a hand written note from 4/19/04 and the other has a hand written note on 4/20/04. On the NCR dated 4/20/04 a hand written "Void" is written across the document. You failed to follow your procedure by not describing disposition of the device on either form. You did not determine if employees needed to be educated on your procedure for handling nonconformances. You failed to determine whether a Corrective Action should be issued.

In your November 24th response to FDA-483 Item #4, it is unclear whether or not you have investigated the reason/reasons for these specific instances of failure. We question how an adequate corrective action plan can be developed without first identifying the reason for system failure. The December response seems to indicate that you disagree that this observation represents a deviation from the Quality System Regulation. We cannot assess the adequacy of this action at this time.

5. **Complaint handling procedures for reviewing and evaluating complaints have not been implemented 820.198(a).**

Your Customer Communication Procedure states the "technical service manager or alternate shall document the analysis and conclusions of inquiry." The procedure also states that "if no analysis is required, the technical service manager or alternate shall document the reason" and it should be in the [redacted] computer system. Twenty-one of 21 complaints reviewed have not had this information documented.

6. **Complaints involving the possible failure of a device to meet any of its specifications were not reviewed, evaluated, and investigated where necessary 21 CFR 820.198(c).**

Specifically,
a) Twenty-one of 21 complaints had no investigation and had no documentation of a reason for not investigating and the individual responsible for the decision.

b) Five of 21 complaints reviewed were for the failure of a water temperature sensor on the Blanketrol 22R. You had not determined why an investigation was not necessary. (Call ID 00738, 00531, 00337, 00764, and 00266)

c) Nine of 21 complaints reviewed were for bubbles in or leaking of the Plastipad blanket. You did not review, evaluate, or investigate the complaints that were received in the last year. In 2002, you initiated an investigation after complaints of bubbles/separation of the same device. According to a memo dated 3/4/02, the recommendation from the investigation was to manufacture the device on a different welding machine. The memo stated the main risk was, "lack of therapy due to water not circulating." You did not document any final determination or corrective action, and you continued to manufacture the device. On 1/29/04 an email sent to management stated the firm would stop taking orders for the device. It also stated that design and manufacturing would work together and may have more devices for stock. You continued to manufacture through 4/2004 without any manufacturing/design changes. You continued to replace failed devices as documented in the nine complaints. (Call ID 0019801, 0026001, 00565, 00591, 00592, 00678, 00676, 00827, and 00824.)

7. **Management with executive responsibility has not ensured that an adequate and effective quality system has been fully implemented and maintained at all levels of the organization 21 CFR 820.20.**

a) For example, you established quality system procedures but failed to ensure the procedures were followed by employees and monitored to maintain the system.

You should know that the deficiencies listed above are serious violations of the law. You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the FDA without further notice. Possible actions include, but are not limited to, seizure, injunction, and/or civil monetary penalties.

Neither this letter nor the FDA-483 that was issued at the conclusion of the inspection is intended to be an all-inclusive list of deficiencies at your facility. As president of Cincinnati Sub-Zero, it is your responsibility to assure adherence to each requirement of the Act and regulations. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be system problems, you must promptly initiate permanent corrective actions.

Please notify this office in writing within fifteen (15) working days of receipt of this letter of the specific steps you have taken to correct the deviations listed above. In addition, please submit any additional documentation to show the corrections initiated in conformance with the requirements of the Quality System Regulation. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the timeframe within which the corrections will be completed.

Federal agencies are advised of the issuance of all Warning Letters about medical devices so that they may take this information into account when considering the award of contracts. Additionally, no requests for Certifications to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

Your written response to this Warning Letter should be sent to Mr. Stephen J. Rabe, Compliance Officer, Food and Drug Administration, 6751 Steger Drive, Cincinnati, Ohio 45237. If you have any questions concerning the contents of this letter, you may contact Mr. Rabe at (513) 679-2700, extension 163, or you may forward a facsimile to him at (513) 679-2773.

Sincerely,

Carol A. Heppe
District Director
Cincinnati District